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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KELLY, ROBERT M	

ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/804,763	QI ET AL.	
	Examiner	Art Unit	
	ROBERT M. KELLY	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-11,18-23 and 25-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-11,18-23 and 25-42* is/are rejected.

7)☐ Claim(s) *22* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/6/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and argument of 2/4/09 are entered.

Claims 1, 7, 11, 18-20, 25, 29, and 30 are amended.

Claims 12, 14, 15, and 24 are cancelled.

Claims 32-42 newly added.

Claims 1, 2, 4-11, 18-23, 25-42 are presently pending.

Election/Restrictions

Claims 1, 2, 4-11, 18-23, 25-42 are presently eligible for consideration for the elected invention and species, with the rejoinder of SEQ ID NO: 2, as it is noted that the other species are no longer specifically claimed.

Claim Status, Cancelled Claims

In light of the cancellation of Claims 12, 14, 15, and 24, the rejections and/or objections to such claims are rendered moot, and thus, are withdrawn.

Claim Objections

Claim 22 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 22 limits only the extracellular domain to CD8alpha chain domain, but specifically encompasses broader embodiments for the transmembrane domain, as

evidenced by the claim language used, as well as the dependent claim, Claim 23 further limiting the transmembrane domain to CD8alpha.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Applicant remains advised that should claim 8 be found allowable, claims 11 and 18 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof, for reasons of record. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 11 and 18 each require specific effects to obtained with the vector of Claim 8, when a cell is transformed with the virus, however, the effects are taught in the specification to be inherent in the vector composition itself, and not to require a distinct structure. Hence, the scope of the composition of Claims 11 and 18 is the same as that of Claim 8, despite a slight difference in wording.

Applicant remains advised that should claim 26 be found allowable, claims 29 and 30 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof, for reasons of record. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 11 and 18 each require specific effects to obtained with the vector of Claim 8, when a cell is transformed with the virus, however, the effects are taught in the specification to be inherent in the vector composition itself, and not to require a distinct structure. Hence, the scope of the composition of Claims 11 and 18 is the same as that of Claim 8, despite a slight difference in wording.

Applicant is newly advised that should claim 32 be found allowable, claim 35 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof, as necessitated by amendment. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim 35 limits the cell as being single or part of a larger collection. Such are the only two possibilities of existence. Hence, despite a slight difference in wording, the claims cover the same scope.

Applicant is advised that should claims 8 or 26 be found allowable, claims 11 and 18 and/or 29 and 30, respectively, will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

The dependent claims are drawn to the vectors being "designed to inhibit" immune responses or responses to the vector, when expressed. However, from the confluence of the specification, it is clear that the mere presence of the CD8alpha chain being expressed on the surface provides such function inherently. Hence, the structure remains unchanged.

Response to Argument – DP warnings

Applicant's argument of 2/4/09 has been fully considered but is not found persuasive.

Applicant argues that functional language may be used to limit a claim, and the claims, as amended, utilize such functional language and hence, there is not DP rejection to be had (pp. 9-10).

Such is not persuasive. The structure of the vectors/polynucleotides remains of the same scope, even with the functional language. The effect desired by such functional language are inherent in the structure of the parent claim in each case.

New Matter Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Separate Expression Requirement

Claims 1, 2, 4-11, 18-23, and 25-30 remain and/or are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for comprising new matter. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In order to curtail frivolous argument, and make the issue crystal clear, the present rejection on the basis of new matter, within the broader classification of written description. Such rejections are the original basis in which the written description developed. The rejection is properly applied when there is no specific contemplation of an amended claim limitation in the original specification and/or original claims. Such does not require any analysis of the prior art, as it rests on the basis as to whether Applicant constructively reduced the invention to practice at the time of filing.

The rejected claims, as listed above, encompass a CD8 alpha-chain coding sequence, and a second sequence encoding a molecule of interest, each linked to control elements directing a generic separate expression of the CD8 alpha chain from that of the molecule of interest.

The specific contemplation of such expression control elements directing separate expression of the two coding sequences is simply not contemplated. Such is not found to be

contemplated as the Examiner cannot explicit or implicit contemplation of such in the specification. To wit, separate expression may be found to be "separate" in several manners. For example, the expression may occur at separate times, or it may be in separate cell types, or it may be separate because translation occurs from separate promoters, or it may be separate because the sequences are separated in expression due to separate translational control elements on a single transcript. Nowhere is this fleshed out in the specification. Moreover, the specification does describe embodiments where the therapeutic molecule is concatenated with the CD8 (paragraph 007, describing antibody binding sites linked to the CD8 alpha chain extracellular domain). However, nowhere is such embodiment excluded from being in the invention, yet it definately cannot be separately expressed.

Hence, due to the number of ways in which "separate expression" can be interpreted, the Artisan would not be able to determine that Applicant had possession of the breadth of the claimed invention at the time of invention.

Further, it is noted that it is Applicant's duty to disclose their support and not the Examiner's duty to find such support.

Response to Argument – New Matter, Separately Expressed

Applicant's argument of 2/4/09 has been fully considered but is not found persuasive.

Applicant argues that paragraph 014 supplies the required support (p. 10, paragraph 5-6).

Such is not persuasive. It states that the polynucleotides may be in separate vectors, or on the same vector, however, such does not exclude the possibility of having the therapeutic protein and CD8alpha chain expressed from the same translational and/or transcriptional control elements.

Applicant argues that paragraph 041 supplies the required support (Id.).

Such is not persuasive. The paragraph again only provides the same support as paragraph 014, although discussing gene therapy protocols.

Applicant argues that paragraph 106 provides the required support (p. 11, paragraph 1).

Such is not persuasive. Paragraph 106 does not limit the possibility of co-expression, and in fact, it provides that the regulatory sequences are not even limited to those stated, which leaves the door open to how they are separately expressed, as discussed in the rejection.

Applicant argues that paragraph 108 provides the required support (Id.).

Such is not persuasive. Paragraph 108 only discusses the possibility of using additional elements for maintainence in two organisms or more.

Applicant should note that the claims do not read on the same and separate vectors, but only a single vector with both polynucleotides being part of such vector. In addition, there is no exclusion of the possibility of the various forms of separate expression discussed in the rejection, and there exists embodiments where the therapeutic molecule is concatenated with the CD8alpha chain. Simply put, there appears to be no support for such separate expression.

Non-Fusion Protein Requirement

In light of the argument, the rejections of Claims 20-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for comprising new matter by way of claiming the CD8 molecule not being a fusion protein are withdrawn.

To wit, paragraph 0067 specifically states that the CD8alpha chain is not a fusion protein.

Old Art Rejections – Withdrawn

Aruffo Reference Rejections

Claim Rejections – 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

In light of the amendments, the rejections of Claims 1, 2, 8, 9, 10, 11, 18, and 19 under 35 U.S.C. 102(b) as being anticipated by US Pat. No. 5,540,926 to Aruffo, et al., as further evidenced by WO 04/042346 to Wohlgemuth, et al. and the previously attached SEQUENCE COMPARISON 1 OF 9/6/06, as demonstrated by e.g., U.S. Patent No. 5,851,806 to Kovesdi, are withdrawn.

To wit, the claims now require that the CD8alpha chain and the therapeutic molecule of interest to be linked to separate transcriptional control elments.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

In light of the amendments, the rejections of Claims 1, 2, 8-11, 18 and 19 under 35 U.S.C. 103(a) as being unpatentable over US Pat. No. 5,540,926 to Aruffo, et al., and US Pat.

No. 6,193,980 to Efstathiou, et al., as further evidenced by WO 04/042346 to Wohlgemuth, et al. and the previously attached SEQUENCE COMPARISON 1 OF 9/6/06, are withdrawn.

To wit, the CD8 is not expressed in a separate transcriptional element from that of the protein of interest.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

In light of the amendments, the rejections of Claims 1, 2, 8-11, 18, and 19 under 35 U.S.C. 103(a) as being unpatentable over US Pat. No. 5,540,926 to Aruffo, et al., and US Pat. No. 6,509,150 Salvetti, et al., as further evidenced by WO 04/042346 to Wohlgemuth, et al. and that attached SEQUENCE COMPARISON 1 OF 9/6/06, are withdrawn.

To wit, Aruffo does not provide for separate transcriptional control elements.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 8, 11, 18, and 19 under 35 U.S.C. 103(a) as being unpatentable over US Pat. No. 5,540,926 to Aruffo, et al., and US Pat. No. 6,207,456 to Baru, et al., as further evidenced by WO 04/042346 to Wohlgemuth, et al. and that attached SEQUENCE COMPARISON 1 OF 9/6/06, are withdrawn.

To wit, Aruffo does not teach separate transcriptional control elements.

Bonyhadi Reference Rejections

Claim Rejections – 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

In light of the amendments, the rejections of Claims 1, 4, 5, 8-11, 18, and 19 under 35 U.S.C. 102(b) as being anticipated by Bonyhadi, et al. (1997) J. Virol., 71(6): 4707-16 are withdrawn.

To wit, Bonyhadi discloses that the proteins are transcribed from a single transcription element.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

In light of the amendment, the rejections of Claims 1, 2, 4, 5, 7-11, and 18-30 under 35 U.S.C. 103(a) as being unpatentable over Zimmer, et al. (1999) Molecular Medicine 5(4): 244-53 and Bonyhadi, et al. (1997) J. Virol., 71(6): 4707-16, are withdrawn.

To wit, Bonyhadi teaches a single transcription of both genes from a single transcriptional control element.

New Art Rejections – Necessitated by Amendment

It should be noted for the follow rejections that "consisting essentially of" continues to be construed as "comprising" (e.g., OA of 11/4/08, p. 15).

It should be noted for the following rejections that the functional language is given no weight, as the structure is met, and hence, the functions would occur.

It should be noted that the pertinent argument is addressed inasmuch as it applies to the present rejections, after all the rejections are recited.

Base Art Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4, 5, 7-11, 18-20, 22, 23, 25-36, 38, 40, and 42 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmer, et al. (1999) Molecular Medicine 5(4): 244-53; Bonyhadi, et al. (1997) J. Virol., 71(6): 4707-16; Gaines, et al. (1999) Biotechniques, 26(4): 683-88; and Grignani, et al. (1998) Cancer Research, 58: 14-19, for reasons necessitated by amendment.

Zimmer teaches the administration of adenoviral vectors comprising the mouse or human ornithine carbamoyl transferase gene, for treatment of mice with OTC deficiency (ABSTRACT).

However, Zimmer does not teach the aspects of such adenoviral vector further comprising a CD8-alpha transgene.

On the other hand, Bonyhadi teaches that a second transgene encoding for the murine homolog of the CD8-alpha chain can be used for detection and/or enrichment of the transformation of the transduced cells (p. 4708, paragraph bridging columns). Further, as noted above, the CD8-alpha gene meets the requirements.

Also, Gaines teaches the use of another cell surface marker for cell sorting of cells expressing a gene of interest (e.g., ABSTRACT).

Still also, Grignani teaches a vector comprising a gene which is used for sorting (GFP), under control of one promoter (CMV), and a further gene of interested, expressed from a separate promoter (5'LTR), as well as even further genes for other selection processes (e.g., PURO) (Figure 1; p. 15, col. 1, paragraph 3; and pp. 16-17, paragraph bridging).

From this it is apparent that the Artisan understands that detection/enrichment/positive selection may be obtained from expression of a protein from the same vector, and further that the

method of production of the vector (from the same promoter/translational control elements) is not something that would give the Artisan cause to question whether it would work.

Hence, it would have been obvious to modify the methods of Zimmer with those of Bonyhadi, to arrive at an adenoviral vector comprising separately translated sequences for CD8-alpha, lacking its cytoplasmic tail, and for ornithine carbamoyl transferase, as further demostrated by Gaines and Grignani. The Artisan would be motivated to do so to monitor and isolate the cells of Zimmer's transformed animals that were transformed, in order to study the amounts of ornithine carbamoyl transferase which was expressed, as taught by Zimmer. Moreover, the Artisan would have had a reasonable expectation of success, Zimmer had shown the method to work, and Bonyhadi had demonstrated that the cells' protein levels could be analyzed and Gaines and Grignani demonstrated that the Artisan understood the methods well enough to select the cells comprising the adenoviral vector by expression from separate transcriptional and translational control elements.

Further modification to utilize human CD8alpha chain

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 4, 5, 7-11, 18-23, 25-36, 38, and 40-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmer, et al. (1999) Molecular Medicine 5(4): 244-53; Bonyhadi, et

al. (1997) J. Virol., 71(6): 4707-16; Gaines, et al. (1999) Biotechniques, 26(4): 683-88; and Grignani, et al. (1998) Cancer Research, 58: 14-19 as applied to claims 1, 4, 5, 7-11, 18-20, 22, 23, 25-36, 38, 40, and 42 above, and further in view of U.S. Patent No. 5,540,926 to Aruffo, et al., as further evidenced by WO 04/042346 to Wohlgemuth, et al. and the previously attached SEQUENCE COMPARISON 1 OF 9/6/06.

As shown above, the various claim limitations are obviated. However, the base references do not teach the use of human CD8alpha, but it is noted that this is recognized by Bonyhadi to be the equivalent protein in humans (p. 4708, paragraph bridging columns).

However, and further, Aruffo teach the use of human CD8alpha for similar isolations (e.g., col. 8, paragraph 5). Further Woholgemuth, et al. teaches the sequence of human CD8alpha.

Hence, at the time of invention, it would have been obvious to further modify these references with the use of human CD8alpha. The Artisan would do so to provide the same function as the murine CD8alpha utilized in the base references. Moreover, the Artisan would have a reasonable expectation of success, as Aruffo utilizes the same isolations with the human CD8alpha, as well as the mere fact that the Artisan did understand that the human version could provide the same function as Bonyhadi's murine CD8alpha, as it is a membrane protein.

Further Modification to Utilize a Synthetic Transmembrane Domain

Claims 1, 2, 4, 5-11, 18-23, 25-36, 38, and 40-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmer, et al. (1999) Molecular Medicine 5(4): 244-53; Bonyhadi, et al. (1997) J. Virol., 71(6): 4707-16; Gaines, et al. (1999) Biotechniques, 26(4): 683-88; Grignani, et

al. (1998) Cancer Research, 58: 14-19; and U.S. Patent No. 5,540,926 to Aruffo, et al, as further evidenced by WO 04/042346 to Wohlgemuth, et al. and the previously attached SEQUENCE COMPARISON 1 OF 9/6/06 as applied to claims 1, 2, 4, 5, 7-11, 18-23, 25-36, 38, and 40-42 above, and further in view of U.S. Patent No. 7,052,906 to Lawson, et al.

As shown above, the various claim limitations are obviated. However, the use of a synthetic transmembrane segment is not suggested.

On the other hand, Lawson teaches a synthetic transmembrane segment which can be utilized for expressing protein on the surface of a protein (e.g., Example 5).

Hence, at the time of invention, it would have been obvious to further modify the invention by use of a synthetic transmembrane domain of Lawson. The Artisan would have been motivated to do so as it served the same function: to link the protein to the surface of the cell. Moreover, the Artisan would have a reasonable expectation of success, as the functionality of the transmembrane segment was shown.

Epithelial Tissue and Nervous System Tissue

Claims 1, 2, 4, 5, 7-11, 18-23, and 25-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmer, et al. (1999) Molecular Medicine 5(4): 244-53; Bonyhadi, et al. (1997) J. Virol., 71(6): 4707-16; Gaines, et al. (1999) Biotechniques, 26(4): 683-88; Grignani, et al. (1998) Cancer Research, 58: 14-19; U.S. Patent No. 5,540,926 to Aruffo, et al., as further evidenced by WO 04/042346 to Wohlgemuth, et al. and the previously attached SEQUENCE COMPARISON 1 OF 9/6/06, and U.S. Patent No. 7,052,906 to Lawson, as applied to claims 1,

2, 4, 5, 7-11, 18-23, 25-36, 38, and 40-42 above, and further in view of U.S. Patent No. 6,303,379, to Selden, et al.

As shown above, the various claim limitations are obviated. However, the epithelial tissue and nervous system tissues are not taught or obviated.

On the other hand, Selden claims transfected primary cells derived of tissues comprising an exogenous nucleic acid, which may encode a therapeutic product (e.g., Claims 1, 6, and 8). Such cells may be *in vivo* and may be, *inter alia,* epithelial cells, neural cells, hepatocytes (e.g., Claim 2), as well as lung fibroblasts (e.g., Example 1). Further the nucleic acid may also comprise a segment encoding a selectable marker (Claim 5), which marker is taught in the specification to include a cell surface marker (e.g., Summary of the Invention, paragraph 6). Still further Selden teaches that the vector may be an adenoviral vector (e.g., section entitled "DNA Constructs").

Hence, it would be further obvious to modify the invention to provide any of Selden's therapeutic transgenes, and transform any of these tissues. The Artisan would be motivated to do so as Selden taught it for transfecting these cells. Moreover, the Artisan would have a reasonable expectation of success, as Selden taught such.

Response to Argument - Art rejections

Applicant's argument of 2/4/09 has been fully considered but does not apply to the present rejections.

Applicant's arguments are that the Art rejections with Aruffo is a fusion protein, and as such Aruffo does not apply (pp. 12-13).

Such does not apply to the present rejections. Aruffo is now applied for a distinct rejection, and the fusion is not pertinent anymore to the rejection.

Applicant argues that Bonyhadi does not teach separate transcriptional control elements (p. 14).

Such does not apply to the new rejections. Bonyhadi is used in combination with other art to demonstrate that the Artisan understood the equivalence of having separate expression control elements.

Applicant argues that neither Zimmer, nor Bonyhadi teach or suggest separate expression (pp. 19-21). Further argued is that the Artisan would arrive at trans-dominant mutants of RevM10, not a therapeutic molecule (Id.).

The Art is now utilized in a new manner. However, RevM10 is a therapeutic molecule as it inhibits HIV replication. How can it not be considered with the broad scope of therapeutic?

Conclusion

No Claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT M. KELLY whose telephone number is (571)272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert M Kelly/
Primary Examiner, Art Unit 1633